

AMENDMENTS TO THE CLAIMS

Claims 12 – 26 are withdrawn pursuant to the restriction requirement.

Please amend claim 1 as shown in the listing of claims.

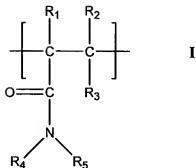
Please add new claim 27.

The listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

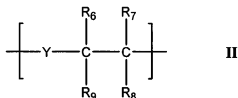
1. (Currently Amended) An innervated artificial tissue comprising:
 - (a) a bio-synthetic matrix comprising a synthetic polymer and a biopolymer, said synthetic polymer comprising one or more N-alkyl or N,N-dialkyl substituted acrylamide co-monomer; one or more hydrophilic co-monomer, or one or more acryl- or methacryl-carboxylic methacryl-carboxylic acid co-monomer derivatised to contain a pendant crosslinkable moiety, or a combination thereof;
 - (b) a plurality of non-nerve cells associated with the bio-synthetic matrix; and
 - (c) a plurality of functional nerve cells associated with the bio-synthetic matrix,

wherein said innervated tissue is formed *in vitro* and wherein said biopolymer is a naturally-occurring polymer.
2. (Currently amended) The innervated artificial tissue according to claim 1, wherein:
 - (i) said N-alkyl or N,N-dialkyl substituted ~~acrylamide~~ acrylamide co-monomer has a structure of Formula I:



wherein: R_1 , R_2 , R_3 , R_4 and R_5 are independently selected from the group of: H and lower alkyl;

- (ii) said hydrophilic co-monomer has a structure of Formula II:



wherein:

Y is 0 or is absent;

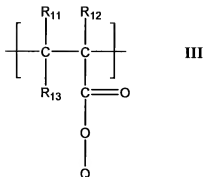
R_6 , and R_7 are independently selected from the group of: H and lower alkyl;

R_8 is H, lower alkyl or $-OR'$, where R' is H or lower alkyl; and

R_9 is H, lower alkyl or $-C(O)R_{10}$, and

R_{10} is $-NR_4R_5$ or $-OR''$, where R'' is H or CH_2CH_2OH ; and

- (iii) said acryl- or methacryl- carboxylic acid co-monomer has a structure of Formula III:



wherein:

R₁₁, R₁₂ and R₁₃ are independently selected from the group of: H and lower alkyl, and

Q is N-succinimido, 3-sulpho-succinimido (sodium salt), N-benzotriazolyl, N-imidazolyl and *p*-nitrophenyl.

3. (Previously amended) The innervated artificial tissue according to claim 1, wherein:

- (i) said one or more N-alkyl or N,N-dialkyl substituted acrylamide co-monomer is selected from the group of: N-methylacrylamide, N-ethylacrylamide, N-isopropylacrylamide (NiPAAm), N-octylacrylamide, N-cyclohexylacrylamide, N-methyl-N-ethylacrylamide, N-methylmethacrylamide, N-ethylmethacrylamide, N-isopropylmethacrylamide, N,N-dimethylacrylamide, NN-diethylacrylamide, N,N-dimethylmethacrylamide, N,N-diethylmethacrylamide, N,N-dicyclohexylacrylamide, N-methyl-N-cyclohexylacrylamide, N-acryloylpyrrolidine, N-vinyl-2-pyrrolidinone, N-methacryloylpyrrolidine, and combinations thereof;
- (ii) said one or more hydrophilic co-monomer is a selected from the group of: acrylic acid, methacrylic acid, 2-hydroxyethyl methacrylate (HEMA), N,N-dimethylacrylamide, N,N-diethylacrylamide, 2-[N,N-dimethylamino]ethylacrylamide, 2-[N,N-diethylamino]ethylacrylamide, N,N-diethylmethacrylamide, 2-[N,N-dimethylamino]ethylmethacrylamide, 2-[N,N-diethylamino]ethylmethacrylamide, N-vinyl-2-pyrrolidinone, 2-[N,N-

diethylamino]ethylacrylate, 2-[N,N-dimethylamino]ethylacrylate, 2-[N,N-diethylamino]ethylmethacrylate, 2-[N,N-dimethylamino]ethylmethacrylate, and combinations thereof; and

- (iii) said one or more acryl- or methacryl- carboxylic acid co-monomer is selected from the group of: acrylic acid, methacrylic acid, or substituted versions thereof, and said cross-linkable moiety is a succinimidyl group, an imidazole, a benzotriazole, a *p*-nitrophenol or 2-(N-morpholino)ethanesulphonic acid.
- 4. (Original) The innervated artificial tissue according to claim 3, wherein said synthetic polymer comprises N,N-dimethylacrylamide and N-acryloxysuccinimide.
- 5. (Original) The innervated artificial tissue according to claim 3, wherein said synthetic polymer comprises N-isopropylacrylamide, acrylic acid and N-acryloxysuccinimide.
- 6. (Original) The innervated artificial tissue according to claim 3, wherein said synthetic polymer comprises N-isopropylacrylamide and acrylic acid.
- 7. (Previously Amended) The innervated artificial tissue according to claim 1, wherein the biopolymer is selected from the group of: collagens, denatured collagens, gelatin, fibrin-fibrinogen, elastin, glycoprotein, alginate, chitosan, hyaluronic acid, chondroitin sulphate, glycosaminoglycan (proteoglycan), and derivatives thereof.
- 8. (Previously Amended) The innervated artificial tissue according to claim 1, wherein said plurality of non-nerve cells are capable of growing as one or more confluent layers over a surface of said bio-synthetic matrix, within the matrix, into the matrix, or a combination thereof.
- 9. (Previously Amended) The innervated artificial tissue according to claim 1, wherein said matrix further comprises one or more bioactive agents.
- 10. (Original) The innervated artificial tissue according to claim 9, wherein the bioactive agent is a pentapeptide having the amino acid sequence YIGSR.

11. (Previously Amended) The innervated artificial tissue according to claim 1, wherein the artificial tissue is formed as an artificial cornea.
12. (Withdrawn) Use of the innervated artificial tissue according to claims 1 for *in vitro* toxicity, irritancy or pharmacological testing.
13. (Withdrawn) Use of a bio-synthetic matrix for the preparation of an innervated artificial tissue, said bio-synthetic matrix comprising a synthetic polymer and a biopolymer, and said synthetic polymer comprising one or more N-alkyl or N,N-dialkyl substituted acrylamide co-monomer; one or more hydrophilic co-monomer, or one or more acryl- or methacryl-carboxylic acid co-monomer derivatised to contain a pendant cross-linkable moiety, or a combination thereof.
14. (Withdrawn) A method of testing cellular effects of a substance *in vitro* comprising:
 - (a) contacting an innervated artificial tissue with a test substance, said artificial tissue comprising
 - (i) a bio-synthetic matrix comprising a synthetic polymer and a biopolymer;
 - (ii) a plurality of non-nerve cells associated with the bio-synthetic matrix; and
 - (iii) a plurality of functional nerve cells associated with the biosynthetic matrix, and
 - (b) determining the effect of the test substance on said plurality of non-nerve cells, said plurality of functional nerve cells, or both.
15. (Withdrawn) An *in vitro* method of toxicology or irritancy testing of a substance comprising:
 - (a) contacting an innervated artificial tissue with a test substance, said artificial tissue comprising
 - (i) a bio-synthetic matrix comprising a synthetic polymer and a biopolymer;
 - (ii) a plurality of non-nerve cells associated with the bio-synthetic matrix; and

- (iii) a plurality of functional nerve cells associated with the biosynthetic matrix, and
 - (b) determining the viability of said plurality of non-nerve cells, said plurality of functional nerve cells, or both.
- 16. (Withdrawn) An in vitro method for investigation of the role of nerves in wound healing comprising:
 - (a) creating a wound in an innervated artificial tissue, said artificial tissue comprising
 - (i) a bio-synthetic matrix comprising a synthetic polymer and a biopolymer;
 - (ii) a plurality of non-nerve cells associated with the bio-synthetic matrix; and
 - (iii) a plurality of functional nerve cells associated with the biosynthetic matrix, said nerve cells being derived from said source, and
 - (b) comparing wound closure rates in said artificial tissue with wound closure rates in an artificial tissue that is not innervated, or in mammalian tissue.
- 17. (Withdrawn) The method according to claim 14, wherein said synthetic polymer comprising one or more N-alkyl or N,N-dialkyl substituted acrylamide co-monomer; one or more hydrophilic co-monomer, or one or more acryl- or methacryl-carboxylic acid co-monomer derivatised to contain a pendant cross-linkable moiety, or a combination thereof.
- 18. (Withdrawn) The method according to claim 17, wherein said synthetic polymer comprises N,N-dimethylacrylamide and N-acryloxysuccinimide.
- 19. (Withdrawn) The method according to claim 17, wherein said synthetic polymer comprises N-isopropylacrylamide, acrylic acid and N-acryloxysuccinimide.
- 20. (Withdrawn) The method according to claim 17, wherein said synthetic polymer comprises N-isopropylacrylamide and acrylic acid.
- 21. (Withdrawn) A method for the innervation of an artificial tissue comprising:

- (a) providing a source of nerve cells; and
 - (b) culturing an artificial tissue in a medium in the presence of said source of nerve cells and one or more compounds that promote nerve growth, whereby nerve cells grow from said source into said artificial tissue, wherein said one or more compounds are present in said artificial tissue or in said medium, or both.
22. (Withdrawn) The method according to claim 21, wherein said one or more compounds that promote nerve growth comprise laminin, nerve growth factor, retinoic acid or retinyl acetate, or a combination thereof.
23. (Withdrawn) The method according to claim 21, further comprising embedding the source of nerve cells in a matrix prior to step (b).
24. (Withdrawn) The method according to claims 21, further comprising embedding the source of nerve cells in said artificial tissue prior to step (b).
25. (Withdrawn) A kit comprising the innervated artificial tissue according to claims 1 and optionally instructions for use.
26. (Withdrawn) A kit for the preparation of an innervated artificial tissue comprising:
- (a) a bio-synthetic matrix comprising a synthetic polymer and a biopolymer, said synthetic polymer comprising one or more N-alkyl or N,N-dialkyl substituted acrylamide co-monomer; one or more hydrophilic co-monomer, or one or more acryl- or methacrylcarboxylic acid co-monomer derivatised to contain a pendant cross-linkable moiety, or a combination thereof; and
 - (b) optionally one or more cell lines, a source of nerve cells, instructions for use, or a combination thereof.

27. (New) The innervated artificial tissue according to claim 1, wherein said biopolymers are derivatized to include functional groups capable of reacting with said pendant crosslinkable moieties of the synthetic polymer.